PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
IRN 639021		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/AU01/00278	14 March 2001	14 March 2000

Applicant

MONASH UNIVERSITY et al

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 6 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

[ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:

[ ] contained in the international application in written form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [X] **Certain claims were found unsearchable** (See Box I).

3. [X] **Unity of invention is lacking** (See Box II).

4. With regard to the **title,**

[X] the text is approved as submitted by the applicant.

[ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**

[X] the text is approved as submitted by the applicant

[ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

[ ] as suggested by the applicant.

[ ] because the applicant failed to suggest a figure

[ ] because this figure better characterizes the invention

[X] None of the figures

INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU01/00278

A. CLASSIFICATION OF SUBJECT MATTER

Int. Cl. [7]: C12N 5/08;

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
SEE ELECTRONIC DATABASES

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
SEE ELECTRONIC DATABASES

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
MedLine CA WPIDS: embryonic stem cells, human, propagation/proliferation, blastocyst, inner cell mass/ICM embryonic stem cells, differentiation, nerve/neural neuronal, stem cell/precursor cell

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	US 6, 200, 806 A (WISCONSIN ALUMNI RESEARCH FOUNDATION) 13/3/01 Whole document	28-40
P,X	WO 00/27995 A (MONASH UNIVERSITY, UNIVERSITY OF SINGAPORE, HADASIT MEDICAL RESEARCH CENTRE) 18/5/00 Whole document	28-61, 63-78
P,Y	WO 00/68359 A (UINIVERSITY OF UTAH RESEARCH FOUNDATION) 16/11/00	28-61, 63-78

[X] Further documents are listed in the continuation of Box C [X] See patent family annex

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
8 May 2001	10 May 2001
Name and mailing address of the ISA/AU	Authorized officer
AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	**Gillian Allen** Telephone No : (02) 6283 2266

INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU01/00278

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	Reubinoff BE et al. Embryonic stem cell lines from human blastocysts: somatic differentiation in vitro. Nature Biotech. 2000. **18**: 399-404	28-61, 63-78
X	Thomson JA et al. Embryonic stem cell lines derived from human blastocysts. Science. 1998. **282**: 1145-47.	28-61, 63-78
X	Brustle O et al. Embryonic stem cell-derived glial precursors: a source of myelinating transplants. Science. 1999. **285**:754-756.	28-61, 63-78
X	Shamblott M et al. Derivation of pluripotent stem cells from cultured human primordial germ cells. Proc Nat Acad Sci USA. 1998. **95**: 13726-731.	39-61, 63-78
X	Svendsen C et al. New prospects for human stem cell therapy in the nervous system. Trends in Neuroscience. 1999. **22**(8): 357-364.	28-61, 63-78
X	Thomson J et al. Neural differentiation of rhesus embryonic stem cells. Acta Pathologica, Microbiologica, et Immunologica Scandinavica. 1998. **106**: 149-157.	39-61, 63-78
X	Lake J-A et al. Reversible programming of pluripotent cell differentiation. J Cell Science. Feb 2000. **113**: 555-66.	39-61, 63-78
X	Thomson J A; Marshall V S. Primate embryonic stem cells. Current Topics in Developmental Biology. 1998. **38** 133-65	28-61, 63-78

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/AU01/00278

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report	Patent Family Member
US 6, 200, 806	AU 47584/96 A
	CA 19960725 A
	EP 19970502 A
WO 00/27995	AU 15150/00 A
WO 00/68359	AU 48262/00 A

END OF ANNEX

INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU01/00278

Box I **Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos :

because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos : **1-27 and 62**

because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

They are not limited to the technical features that define the invention, namely methods for culture and differentiation of human embryonic stem cells to produce neural precursor cells, neurons or glial cells

3. ☐ Claims Nos :

because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)

Box II **Observations where unity of invention is lacking (Continuation of item 3 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

This authority found that the claims were to 7 separate inventions. After taking into account the unsearchable claims (Box I above), the authority found two main inventions. See extra sheet, continuation of Box II, for details.

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☒ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU01/00278

Supplemental Box
(To be used when the space in any of Boxes I to VIII is not sufficient)

Continuation of Box No: II Unity of Invention

The International searching Authority has found 7 separate inventions as identified below.

1. An enriched population of human undifferentiated embryonic stem cells that can be proliferated and differentiated into neural progenitor cells. Invention 1 is defined by claims 1-3.

2. An undifferentiated human embryonic stem cell, not limited to the enriched culture of claim 1. The cell is defined as carrying well known human pluripotent markers Invention 2 is defined by claims 4-7.

3. A differentiated committed human cell progenitor line, capable of differentiation and propagation into neural cells, not limited to having been produced from inventions 1 or 2. Invention 3 is defined by claims 8-27.

4. A method of preparing undifferentiated human stem cells that is not limited to the cells or cultures of inventions 1-3, and embryonic stem cells prepared by this method. The method step are limited to using blastocyst ICM as a source of embryonic stem cell material, and culturing it under conditions that promote proliferation of undifferentiated stem cells. Invention 4 is defined by claims 28-38 and 57-61.

5 A method of inducing somatic differentiation of stem cells, and differentiated cells produced by this method, where the stem cells are not limited to those of any of the previous inventions. The culture methods are limited to providing a differentiating signal under conditions that predispose towards production of somatic cells. Invention 5 is defined by claims 39-44, 63, part 64-67, 68-71, and part 72-76.

6. A method of inducing somatic cells from embryonic stem cell derived somatic progenitors, where the somatic progenitors are not limited to those of invention 5 or 3. The claim is limited to the non-novel feature of culture on an adhesive substrate. Apart from that feature, the culture conditions are defined only by the result, ie differentiation into somatic cells. Invention 6 is defined by claims 45-56.

7. A method of transplanting ES derived neural progenitor spheres, where the spheres are not limited to having been derived from or produced by any of inventions 1-6. The method is defined by disaggregation of the spheres and injection. Invention 7 is defined by claims 62, part 64-67 and part 72-76.

The only feature that unites all the claims is that the cells, cell lines and methods are to embryonic stem cells, or to cells derived from embryonic stem cells. However embryonic stem cells are not novel. There is therefore no special technical feature that unites the different inventions, as required by rule 13.2 of the PCT.

It is considered that there are two main inventions

A. specific methods for culturing and proliferating undifferentiated embryonic stem cells from blastocyst inner cell mass. Invention 4 encompasses but is not limited to this invention. This invention would include cells produced by the specific culture methods.

B. specific methods for differentiating embryonic stem cells into neural precursors, and hence into neural or glial cells. Inventions 5-6 encompass but are not limited to this invention. This invention would include cells produced by the specific culture methods.